REMARKS/ARGUMENTS

Reconsideration and continued examination of the above-identified application are respectfully requested.

Claims 25 and 27-28 are pending. Claim 25 has been amended to incorporate the limitations of claim 26. Claim 25 has been further amended to recite the step of determining the amino acids encoded at positions 57 and 67 of the HLA DQB1* gene of the patient and to recite the step of determining that immunotherapy will have a statistically significant probability of prolonging the cancer patient's survival when Asp is encoded at position 57 of the HLA DQB1* gene of the patient and Val is encoded at position 67 of the HLA DQB1* gene of the patient. Claim 26 has been canceled. Claims 27-28 have been withdrawn previously. Full support for the amendments to claim 25 can be found throughout the present application, for instance, at pages 24-27 and in Figs. 4, 5, and 6. Accordingly, no questions of new matter should arise and entry of this amendment is respectfully requested.

Objection to the Specification

At pages 2-3 of the Office Action, the Examiner objects to the disclosure because the Examiner states that it is unclear what is meant by the letter symbols that appear in the specification and the drawings.

As described in the present application, the upper case letters shown in the figures are single character codes of amino acids (See present application, page 18). The present application analyzes the influence of the variations of amino acids on metastases and treatment. Amino acid positions which are associated with a statistically significant difference in treatment have been identified for each given treatment by the amino acid type (heterozygote or homozygote) (See

present application, page 25). Thus, in Fig. 34, FF at position 9 would indicate a homozygote (both copies of the gene code for F at position 9) and FL at position 9 would indicate a heterozygote (one copy of the gene codes for F and one copy of the gene codes for L at position 9). Fig. 34 reveals that immunotherapy is not suitable for a patient with FL at position 9 of the amino acid sequence on DQB1* gene. As such, it is respectfully submitted that the specification does define the symbols used in the figures and one of ordinary skill in the art would be able to understand the figures based on this definition. Accordingly, this objection should be withdrawn.

Rejection of Claim 25 Under 35 U.S.C. §112, Second Paragraph

At pages 3-4 of the Office Action, the Examiner rejects claim 25 under 35 U.S.C. §112, second paragraph. The Examiner states that the specification, while being enabling for correlating genetic polymorphisms of three specific genes with stomach cancer treatment, does not reasonably provide enablement for correlating genetic polymorphisms of the three specific genes with any cancer. This rejection is respectfully traversed.

Claim 25 complies with the requirements of 35 U.S.C. §112, second paragraph. In order to assist the Examiner, however, claim 25 has been amended to incorporate the limitations of claim 26. As such, claim 25 as presently amended recites that the cancer of the patient comprises stomach cancer. As acknowledged by the Examiner, the specification is enabling for correlating genetic polymorphisms with stomach cancer treatment.

Accordingly, this rejection should be withdrawn.

Rejection of Claims 25-26 Under 35 U.S.C. §112, second paragraph

At pages 5-6 of the Office Action, the Examiner rejects claims 25-26 under 35 U.S.C. §112,

second paragraph. The Examiner states that it is not clear whether the phrase "one or more of positions" recited in the claim refers to positions along the nucleotide sequence or positions along the amino acid sequence. The Examiner also states that claim 25 recites a method for determining cancer treatment based on the amino acids encoded at particular positions of three different particular class II HLS genes. The Examiner states that it is unclear how the determined amino acids encoded at particular positions of the three distinct genes affects the determination of a cancer treatment. This rejection is respectfully traversed.

Claims 25-26 comply with the requirements of 35 U.S.C. §112, second paragraph. In order to assist the Examiner, however, claim 25 has been amended to incorporate the limitations of claim 26 and to recite, in part, the step of determining the amino acids encoded at positions 57 and 67 of the HLA DQB1* gene of the patient. The phrase "one or more of positions" has been deleted from the claim. Claim 25 has been further amended to recite the step of determining immunotherapy to have a statistically significant probability of prolonging the cancer patient's survival when Asp is encoded at position 57 of the HLA DQB1* gene of the patient and Val is encoded at position 67 of the HLA DQB1* gene of the patient. The present application clearly describes the association of immunotherapy with prolonged survival of patients with DQRB*105031 gene (Asp at position 57, Val at position 67). As shown in Fig. 6 of the present application, survival rates of patients with DQRB*105031 gene (Asp at position 57, Val at position 67) with anti-cancer immunotherapy after cancer resection, has been found to be statistically longer than patients without the gene (five-year survival rates were 90% and 50% in patients with positive and negative DQRB* 105031 gene, respectively). As further described at pages 26-27 of the present application, if patients could be confirmed as not having DQRB* 105031 gene (Asp at position 57, other than Val at position 67), immunotherapy would not be a

recommended treatment for them. The present claims as amended, comply with the requirements of 35 U.S.C. §112, second paragraph.

Accordingly, this rejection should be withdrawn.

Rejection of Claims 25-26 under 35 U.S.C. §103(a) -- Davies et al. in view of Bateman et al. and further in view of Lee et al. and further in view of Santamaria et al. as evidence by Lv et al. and NCBI.

At pages 7-13 of the present application, the Examiner states that claims 25-26 are rejected under 35 U.S.C. § 103 (a), as being unpatentable over Davies et al. (J. CLINICAL ONCOLOGY, Vol. 19, pp. 1279-87, 2001) in view of Bateman et al. (JOURNAL OF PATHOLOGY, Vol. 188, pp. 231-236, 1999) and further in view of Lee et al. (GASTROENTEROLOGY, Vol. 111, pp. 426-432, 1996) and further in view of Santamaria et al. (U.S. Patent No. 5,972,604) as evidenced by F.Lv et al. (TISSUE ANTIGENS, Vol. 64, pp. 512-514, 2004) and NCBI. The Examiner states that Davies et al. teaches a method for evaluating cancer treatments based on genotyping polymorphic genes of patients receiving cancer therapy and correlating the survival results of patients containing a specific polymorphic gene with appropriate cancer treatment regimens. The Examiner acknowledges that Davies et al. does not teach any association of HLA class II genes with any cancer. The Examiner states that Bateman et al. specifically discusses the DQB1, DRB1, and DPB1 genes and alleles and their associations with particular cancers. The Examiner states that Bateman et al. further states that HLA genotypes may help to predict treatment success in cancer patients. The Examiner further acknowledges that Bateman et al. does not specifically teach correlations between the specific HLA class II genes and stomach cancer or treatment. The Examiner states, however, that the references of Lee et al. and Santamaria et al. teach that HLA Class II genes are associated with several cancers. The Examiner states that it would have been *prima facie* obvious to one of ordinary skill in the art

to use the genotyping methods of Davies et al. or Lee et al. or Santamaria et al. along with the statistical methods of Davies et al. to identify HLA Class II polymorphic genes of patients receiving cancer therapy and correlating the survival results of HLA Class II genotyping with appropriate cancer treatment regimens as suggested by Bateman et al. This rejection is respectfully traversed.

The cited references do not teach or suggest the method of the present claims. In order to assist the Examiner, however, claim 25 has been amended to recite that the cancer to be treated is stomach cancer and to recite the step of determining the amino acids encoded at positions 57 and 67 of the HLA DQB1* gene of the patient. Claim 25 has been further amended to recite the step of determining that immunotherapy will have a statistically significant probability of prolonging the cancer patient's survival when Asp is encoded at position 57 of the HLA DQB1* gene of the patient and Val is encoded at position 67 of the HLA DQB1* gene of the patient. The cited references do not, alone or in combination, teach or suggest the presently amended claims. It is further noted that the cited references do not provide any indication whatsoever that position 57 of the HLA DQB1* gene of a patient or position 67 of the HLA DQB1* gene of the patient has any relationship at all with any type of cancer treatment. Consequently, one of ordinary skill in the art could not arrive at the present claims without undue experimentation. Accordingly, this rejection should be withdrawn.

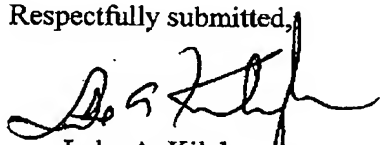
CONCLUSION

In view of the foregoing remarks, the applicant respectfully requests the reconsideration of this application and the timely allowance of the pending claims.

If there are any fees due in connection with the filing of this Amendment, please charge the fees to Deposit Account No. 50-0925. If a fee is required for an extension of time under 37

C.F.R. §1.136 not accounted for above, such extension is requested and should also be charged to our Deposit Account.

Respectfully submitted,



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